Amendments to the Claims

This listing of clams will replace all prior version, listings, of claims in the specification:

Listing of Claims:

1. (original) A method of screening for and /or diagnosis of a cardiovascular disorder in a subject, comprising the steps of:
   a) detecting and /or quantifying the level of a polypeptide in a biological sample from said subject, wherein the polypeptide is selected from:
      i) a polypeptide comprising the amino acid sequence selected from the group consisting of: Cardiovascular disorder Plasma Polypeptides (CPPs) 149-402;
      ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence selected from the group consisting of: CPPs 149-402; and
      iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long, and
   b) comparing said level to that of a control sample, wherein an increase in said level relative to that of the control is indicative of a cardiovascular disorder.

2. (original) A method of predicting a cardiovascular disorder in a subject, comprising the steps of:
   a) detecting and for quantifying the level of a polypeptide in a biological sample from said subject, wherein the polypeptide is selected from:
      i) a polypeptide comprising the amino acid sequence selected from the group consisting of: Cardiovascular disorder Plasma Polypeptides (CPPs) 149-402;
      ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence selected from the group consisting of: CPPs 149-402; and
      iii) a fragment of a polypeptide as determined in i) or ii) above which is a least ten amino acids long; and
   b) comparing said level to that of a control sample, wherein an increase in said level relative to that of the control indicates a risk of developing a cardiovascular disorder.

3. (currently amended) The method of claim 1 ~~or 2~~, wherein said cardiovascular disorder is Coronary Artery Disease (CAD).

4 (currently amended) The method of ~~any one of claims 1-3~~ claim 1, wherein said biological sample is plasma.

5. (currently amended) The method of ~~any one of claims 1-4~~ claim 1, wherein said method is performed *ex vivo*.

6. (currently amended) The method of ~~any one of claims 1-5~~ claim 1, wherein said polypeptide is detected and /or quantified by mass spectrometry.

7. (currently amended) The method of ~~any one of claims 1 to 5~~ claim 1, wherein said polypeptide is detected and /or quantified by Enzyme-Linked Immuno Sorbent Assay.

8. (original) An isolated polypeptide comprising the amino acid sequence selected from the group consisting of Cardiovascular disorder Plasma Polypeptide (CPP) 149-402, wherein said polypeptide is fused to a heterologous polypeptide sequence 9 An anti-Cardiovascular disorder Plasma Polypeptide (CPP) antibody that selectively binds to a polypeptide comprising the amino acid sequence selected from the group consisting of CPPs 149-402.

9. (original) An anti-Cardiovasular disorder Plasma Polypeptide (CPP) antibody that selectively binds to a polypeptide comprising the amino acid sequence selected from the group consisting of CPPs 149-402.

10. (cancelled) A method of binding an antibody to a Cardiovascular disorder Plasma Polypeptide (CPP) comprising the steps of:

i) contacting the antibody of claim 9 with a biological sample under conditions that permit antibody binding; and

ii) removing contaminants.

11. (cancelled) The method of claim 10, wherein said antibody is attached to a label group.

12. (cancelled) The method of claim 10, wherein said sample is human plasma.

13. (cancelled) A method of identifying a Cardiovascular disorder Plasma Polypeptide (CPP) modulator comprising the steps of:

i) contacting a test compound with a polypeptide selected from the group consisting of CPPs 149-402 under sample conditions permissive for at least one CPP biological activity;

ii) determining the level of said at least one CPP biological activity;

iii) comparing said level to that of a control sample lacking said test compound; and

iv) selecting a test compound which causes said level to change for further testing as a CPP modulator for the prophylactic and/or therapeutic treatment of cardiovascular disorders.

14. (original) An isolated polypeptide having the amino acid sequence of Cardiovascular disorder Plasma Polypeptide (CPP) selected from the group consisting of CPP 154, 155, 181-192, 197, 198, 210, 214,258-268,273, 275- 289, 292, 294-297, 302-402.

15. (original) An isolated polynucleotide encoding the polypeptide of claim 14.

16. (cancelled) A method of identifying a modulator of a cardiovascular disorder comprising the steps of:

(a) administering a candidate agent to a non- human test animal which is predisposed to be affected or which is affected by the cardiovascular disorder;

(b) administering the candidate agent of (a) to a matched control non-human animal not predisposed to be affected or not being affected by the cardiovascular disorder;

(c) detecting and /or quantifying the level of a polypeptide in a biological sample obtained from the non-human test animal of step (a) and from the control animal of step (b), wherein the polypeptide is selected from

i) a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequences listed in Table 3 (CPPs 149-402);

ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to an amino acid sequence selected from the group consisting of the amino acid sequences listed in Table 3 (CPPs 149 402); and iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long; and

(d) comparing the levels of the polypeptide of step (c); wherein a displacement of the level of the polypeptide in the biological sample obtained from the non-human test animal towards the level of the polypeptide in the biological sample obtained from the control animal indicates that the candidate agent is a modulator of the cardiovascular disorder.

17. (cancelled) The method of claim 16, wherein the non-human test animal which is predisposed to be affected or which is affected by the cardiovascular disorder comprises an increased plasma level of a polypeptide selected from:

i) a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequences listed in Table 3 (CPPs 149-402);

ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to an amino acid sequence selected from the group consisting of the amino acid sequences listed in Table 3 (CPPs 149-402), and

iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long.

18. (cancelled) A method for monitoring the efficacy of a treatment of a subject having or at risk of developing a cardiovascular disorder with an agent, the method comprising:

(a) obtaining a pre-administration biological sample from the subject prior to administration of the agent;

(b) detecting and /or quantifying the level of a polypeptide in the biological sample from said subject, wherein the polypeptide is selected from:

i) a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequences listed in Table 3 (CPPs 149-402);

ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to an amino acid sequence selected from the group consisting of the amino acid sequences listed in Table 3 (CPPs 149 402); and

iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long; and

(c) obtaining one or more post-administration biological samples from the subject;

(d) detecting the level of the polypeptide in the post-administration sample or samples;

(e) comparing the level of the polypeptide in the pre-administration sample with the level of the polypeptide in the post-administration sample; and

(f) adjusting the administration of the agent accordingly.

19. (cancelled) A method for the treatment of biliary cirrhosis, gallstones, celiac disease or symptoms and conditions associated with intestinal motility disorders comprising administering an effective amount of a CPP 232 polypeptide to a mammal, including a human, suffering from said disease.

20. (cancelled) The method of claim 19 wherein the intestinal motility disorder is a gastrointestinal motility disorders selected from the group consisting of Irritable bowel syndrome, Diabetes, Gastroparesis, Esophageal spasms, Hirschsprung's disease, Chronic intestinal pseudo- obstruction, Scleroderma and Achalasia.

21. (cancelled) The method of claim 19 wherein the symptoms associated with intestinal motility disorders is a symptom selected from the group consisting of difficulty in swallowing, heartburn, gas, bloating, nausea, vomiting, constipation and diarrhea.

22. (cancelled) A method of identifying a modulator of biliary cirrhosis, gallstones, celiac disease or symptoms and conditions associated with intestinal motility disorders comprising

i) contacting a test compound with CPP 232 under sample conditions permissive for CPP 232 biological activity;
ii) determining the level of said CPP 232 biological activity;
iii) comparing said level to that of a control sample lacking said test compound; and
iv) selecting a test compound which causes said level to change for further testing as a CPP 232 modulator for the prophylactic and/or therapeutic treatment of biliary cirrhosis, gallstones, celiac disease or symptoms and conditions associated with intestinal motility disorders.

23. (cancelled) A method according to claim 22, wherein the level of CPP 232 biological activity is measured by determining the level of expression of one or more genes set forth in Table 4.

24. (cancelled) A method for the prognosis or diagnosis of a gallstone or celiac disease comprising detecting the plasma level of CPP 232, wherein an increased level is indicative of biliary cirrhosis, gallstones, celiac disease or symptoms and conditions associated with intestinal motility disorders.

25. (cancelled) A method for the prognosis or diagnosis of biliary cirrhosis, gallstones, celiac disease or symptoms and conditions associated with intestinal motility disorders comprising

i) detecting a level of expression of at least one gene identified in Table 4 in a sample of a suitable tissue obtained from the subject to provide a first value; and

ii) comparing the first value with a level of expression of the said gene from a disease free subject, wherein a greater or smaller expression level in the subject sample compared to the sample from the disease-free subject is indicative of the subject being predisposed to or having biliary cirrhosis, gallstones, celiac disease or symptoms and conditions associated with intestinal motility disorders.

26. (cancelled) The method of claim 25, wherein the level of expression of at least two, at least three, at least four or at least five genes identified in Tables 4 is detected.

27. (cancelled) A method according to claim 19 to 26, wherein said CPP 232 is a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to an amino acid sequence set forth in SEQ ID No: 706.